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The physiological action of the heavy oil of wine

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THE PHYSIOLOGICAL ACTION OF THE HEAVY OIL OF WINE.

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THE heavy oil of wine, as one of the component parts of Hoffmann's anodyne, occupies a prominent but an unrecognized place in our list of remedies.

According to the U. S. Dispensatory, this agent is formed by the distillation of alcohol with a large excess of sulphuric acid. The product of the distillation is generally in two layers, one of which contains the heavy oil of wine, while the other layer consists of sulphurous acid. For the purpose of separating any ether which may be in the oily layer, it is exposed to the air for twenty-four hours, when it is washed with water, thereby removing any sulphurous acid which may contaminate it, and after these two processes have been accomplished the oil is ready for the market. Notwithstanding the fact that Hoffmann's anodyne is so frequently used, and has for so long a time occupied a prominent place in the household, and a useful one in the profession, curiously enough, nothing seems to have

been done toward increasing our knowledge of its composition or of its physiological effects. Its formation is generally accounted for in the following manner:

When sulphuric acid and alcohol are added together, one of the results of their union is sulphovinic acid ($C_2H_5HSO_4$); but if the sulphuric acid be in great excess the sulphovinic acid is partially decomposed, forming the heavy oil of wine.[1] The mixture now consists of ethyl-sulphate, $(C_2H_5)_2SO_4$; ethyl-sulphite, $(C_2H_5)_2SO_3$; and ethyline, C_2H_4. Two forms of this ethyline are known, viz., etherin and etherol, and the mixture of these two separate forms of ethyline alone, forms the *light oil of wine*.

The same doubt seems connected with the specific gravity of the heavy oil. Sadtler believes 1.133 to be the most correct estimation of its specific gravity yet made.

At the suggestion of Dr. H. C. Wood, I performed the following experiments in order to discover what part was played by the oil when administered with alcohol and ether in Hoffmann's anodyne. Of course, under the latter circumstances the action of the oil is entirely subservient to and masked by the more rapidly acting and more diffusible stimulants; but the results of the following investigations were, at least, marked enough to show that the drug before us occupies no mean position in the anodyne mixture. Starting with the object of seeing in what manner the circulation is influenced, and beginning with the heart of the frog, the following results arose from my investigations:

When the isolated heart of the frog is placed in

[1] Dr. Squibb believes the heavy oil of wine to be a sulphovinate of a hydrocarbon radical.

the pure oil the rapidity of its movements is increased very distinctly (about ten beats more a minute) for some moments; following this stage of stimulation comes a condition of exhaustion or depression, during which the cardiac movements are imperfectly performed, with a constantly increasing feebleness, and finally the viscus stops in diastolic collapse.

Seven other experiments with the isolated heart now followed, a weaker solution of the oil being used in each experiment, and it became evident that the duration of the period of stimulation was in inverse ratio to the size of the dose, so that the seventh heart had its increased rapidity of movement continued for a longer period than any of its predecessors. The action of the drug when dropped in varying strengths upon the heart when lying in its pericardial sac was identical with its effects upon the isolated viscus, so far as the eye could discern. Unfortunately, any study as to the relative propelling power of the heart when under the influence of the oil was impossible, owing to the fact that no frogs of sufficient size were obtainable; the hearts I was obliged to use being too small for use in any of the so-called frog manometers. It is evident, however, that in small and ordinary quantities the heavy oil of wine is a cardiac stimulant, while overwhelming doses are needed to produce cardiac depression.

The experiments made on the higher animals—the dog, for example—showed that the drug affects the mammalian circulatory system in much the same manner as it does that of the frog. It will be seen from the accompanying table and tracings that small doses of the oil (2 to 7 minims) increase pulse-rate, force, and pressure, while larger doses (1 to 2 c. c.) decrease pressure to a considerable extent; exceed-

ingly large doses seem necessary to depress the heart. Indeed, the perfect vasomotor palsy resulting from large doses of the oil would seem to point to the conclusion that the heart stops rather because its vital centres do not receive a sufficient quantity of fluid for their maintenance, than to a direct depressing action of the drug on that viscus, for it has already been shown that overwhelming doses are necessary to depress the heart of the frog, and one of the subjoined tracings shows how much power remains in the heart even when the *arterial pressure* is not more than 5 mm. above the abscissa line.

DOG; WEIGHT 20 POUNDS; CURARIZED; ARTIFICIAL RESPIRATION.

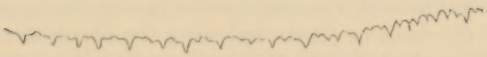
Time.	Drug.	Pressure.	Pulse.	
12.20	.....	134	186	
12.20.10	2 min.	134	192	Injection begun.
12.20.20	.....	146	192	Injection ended.
12.20.30	.....	144	192	
12.20.40	.....	144–150	186	
12.20.50	.....	130–150	240	
12.22	.....	164	186	
12.22.10	4 min.	150–180	192	Injection begun.
12.22.20	.....	180	180	
12.22.30	.....	170–160	198	Injection ended.
12.22.40	.....	160	194	

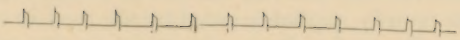
A brief glance at the experiments so far performed shows that this oil produces on the circulation the following effects:

1st. Small doses increase arterial pressure.
2d. Large doses decrease arterial pressure.
3d. Small doses increase rate.
4th. Very large doses are required to diminish rate.
5th. Small doses increase force.
6th. Large doses do not decrease force.

7th. That it requires very large doses, indeed, materially to decrease force.

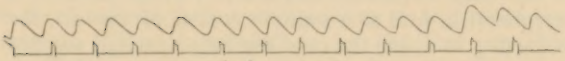
TRACING No. 1.





Showing rate and pressure in normal dog.

TRACING No. 2.



Showing rate and fall of pressure produced by 10 c. c. of the oil injected into jugular. The increased height of the pulse wave over the normal is always present when the vaso-motor system is depressed and the heart is not.

*

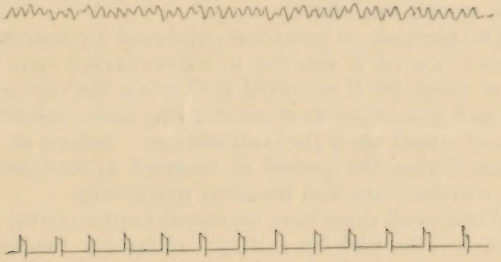
The questions now arising, limit themselves to the consideration and the elucidation of these results, and each one was examined in the above order and individually.

It was proved, by careful and repeated observation, that the rise in pressure following the administration of from 2 to 7 minims of the oil was due in no way to a respiratory action of the drug, for in the curarized animal the rise was as great as in the dog, the respiratory functions of which were not interfered with, and there are, therefore, but three modes of explaining this increase of pressure. Either the vasomotor system is stimulated centrically or peripherally, or cardiac force is sufficiently increased to produce a general rise in pressure. As every one knows, this latter condition is scarcely ever met with in an unalloyed state, a vasomotor stimulation generally accompanying increased cardiac force.

Few drugs also produce peripheral vasomotor excitability, without affecting the higher vasomotor centres in the fourth ventricle. It was proved by two experiments in which the spinal cord of a dog was severed high up in the cervical region, thereby causing a complete cutting off of any impulses from the centres, that this rise was due to a centric action of the remedy, probably aided by the cardiac stimulation, for under these circumstances no rise of pressure took place when the drug was given. The decrease in arterial pressure produced by large doses of the drug evidently depends, in great part, on a peripheral as well as a centric action of the oil, for in the dog in which the cord was intact the fall was not as great as in the animal the cord of which was divided. It would, therefore, seem probable that the drug in large doses affects the centres to but a slight extent, for if its dominant action under such circumstances

was centric, we should expect to find as great a degree of fall when the cord was intact as when it was cut. The extreme difficulty surrounding all efforts to decide whether the peripheral vasomotor action of a drug is alone the cause of a fall of pressure, prevents our absolute decision on this point. While we cannot, therefore, state that the heavy oil of wine paralyzes the centres or periphery, singly and individually, we can rest assured that it does, in large doses, depress the peripheral ends of the vasomotor nerves. (See tracings numbers 3 and 4.)

TRACING NO. 3.

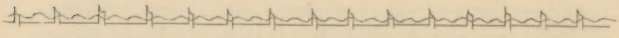


Cord cut: normal tracing.

In regard to the increase in pulse-rate following small and moderate sized doses of the oil, we find that it is probably due to a direct cardiac stimulation, rather than to any depressing action on the inhibitory nerves. This is pointed to by the fact that the rapidity of movement in the frog's heart when isolated was increased by the drug, and also by the fact that section of these inhibitory nerves invariably caused an increase in rate of so decided a charac-

ter, that any previous vagal depression could hardly be present. Further than this, other experiments showed that when section of the vagi and cord was synchronously made, thus leaving the heart free from

TRACING NO. 4.



Cord cut: showing complete vasomotor palsy produced by 4½ c. c. of the oil.

all nervous influences of a centric character, the same increase in rate took place as when the cardiac nervous system was intact.

The decrease in pulse-rate produced by enormous doses of the oil is also due to a direct effect upon the heart itself, for it occurred both when the vagi were cut and when they were whole; the same condition also obtained when the cord was cut. Section of the vagus during the period of decrease in rate caused but a momentary and transient quickening.

When small doses have increased cardiac force, the force is increased by a direct action on the heart muscle or its ganglia; or, in other words, the stimulation which increases rate also increases force. This is rendered the more likely by the fact that cardiac force remains almost as long as cardiac rate is increased, or at least until the rapid rate is no longer one of power, but of weakness.

Very large doses cause decrease in heart power by a direct action on the heart muscle, and by producing such a general vasomotor palsy that the heart cannot obtain a sufficient quantity of blood to enable it to drive out through the hungry bloodvessels a fair-sized pulse-wave. The heavy oil of wine in the dose of 3

TRACING NO. 5.

Normal tracing.

c. c. to a very strong and powerful dog weighing 25 pounds, increased the force and rapidity of his respirations very markedly, as may be seen from tracings

numbers 5 and 6. Violent spasmodic efforts at forcible breathing came on after the administration of a

TRACING NO. 6.

Showing increased respiratory rate after 3 c. c. of the oil.

second dose, but as these severe respiratory changes did not occur in other dogs under like circumstances, I believe them to be due to the plugging up of the minute bloodvessels near the respiratory centres by minute oily emboli.

On the nervous system the drug seems to exert but little influence, for even when given in enormous doses to frogs no nervous phenomena were developed, and careful electrical studies on the nerves and muscles when in contact with the oil failed to show any signs of action of the drug.

While the writer was unable to demonstrate any nervous effects produced by the oil of wine, he does not wish it thought that he denies that such influence exists, although he believes it to be very slight indeed. From his experiments it seems probable that

First. The belief in heavy oil of wine being the quieting agent in Hoffmann's anodyne, is fallacious.

Second. That the calmative effects of this mixture depend largely on the ether, rather than on the oil.

Third. It would seem probable that in Hoffmann's anodyne we possess an agent in which there are linked together three drugs of undoubted power, each one of which successively substitutes the other, stimulating the system in the order here named, viz., ether, alcohol, and the heavy oil of wine.

On animal temperature, as ascertained by the thermometer in the rectum, no effect is produced, even when the arterial pressure is very low. That large doses of the heavy oil of wine are in no way possessed of toxic effects, was proved by the fact that 30 c. c. of the drug given by the mouth to a small dog, weighing 12 pounds, failed to produce any apparent symptoms, except, perhaps, to stimulate him slightly. While the odor of the oil is penetrating, it is by no means disagreeable, and it possesses but little taste other than that of the presence of an oily substance.